AMENDMENTS TO THE CLAIMS

This listing of the claims will replace all prior versions, and listings, of claims in this application.

Listing of Claims

1. (Currently Amended) A method of measuring the ability of a test compound which is an inhibitor of a biological target to inactivate the ~~a~~ biological target in a cell of a subject, comprising the steps of:
(a) administering the test compound to a subject, such that any of the biological target in the subject's body which reacts with the test compound is inactivated and any of the biological target which does not react with the test compound is free;
(b) removing a plurality of ~~a~~ biological samples ~~comprising one or more cell types~~ from the subject~~;~~, wherein each of the plurality of biological samples is derived from a different tissue of the subject;
(c) determining the amount of the free biological target within each of the plurality of biological samples, ~~sample or a~~ fractions thereof; and
(d) comparing the amounts ~~amount~~ determined in step (c) with the amount of free biological target in a control sample,
wherein a decrease in the amount of free biological target each of the biological samples determined in step (c) compared to the amount determined in the control sample provides a measure of the amount of inactivated biological target in each of the biological samples, or fractions thereof.

2. (Currently Amended) The method of Claim 1 wherein the amount of free biological target is determined by measuring the activity of the biological target ~~biomolecule~~ within each of the biological samples or fractions thereof.

3. (Currently Amended) The method of Claim 1, wherein the amount of free biological target is determined by a method comprising the steps of:
(i) contacting each of the biological samples, or a fractions thereof, with a saturating amount of a quantifiable irreversible inhibitor of the biological target, so that substantially all of the free biological target reacts with the quantifiable irreversible biological target inhibitor to form a target/inhibitor complex; and
(ii) determining the amount of target/inhibitor complex formed in step (i).

4. (Original) The method of Claim 1 wherein the biological target is an enzyme, a g-protein coupled receptor, a cytokine, or a receptor kinase.

5. (Original) The method of Claim 4 wherein the biological target is MetAP-2.

6. (Currently Amended) A method for determining the extent of inactivation of MetAP-2 in a biological sample, or fraction thereof, derived from a subject, comprising the steps of:
(a) administering a test compound which is an inhibitor of MetAP-2 to the subject, wherein any MetAP-2 in the body of the subject that reacts with the test compound is inactivated MetAP-2 and any MetAP-2 that does not react with the test compound is free MetAP-2;
(b) removing a plurality of ~~a~~ biological samples ~~comprising one or more cell types~~ from the subject~~;~~, wherein each of the plurality of biological samples is derived from a different tissue of the subject; and
(c) determining the amount of free MetAP-2 within each of plurality of ~~in~~ the biological samples, ~~sample~~ or ~~a~~ fractions thereof; and
(d) comparing the amounts ~~amount~~ determined in step (c) with the amount determined in a control sample;
wherein a decrease in the amounts in each of the biological samples ~~amount~~ determined in step (c) compared to the amount determined in step (d) is a measure of the extent of inactivation of MetAP-2 in each of the biological samples, or fractions thereof.

7. (Currently Amended) The method of Claim 6 wherein the amount of free MetAP-2 is determined using a method comprising the steps of:
(i) contacting at least a portion of each of the biological samples with a saturating amount of a quantifiable irreversible MetAP-2 inhibitor, whereby substantially all of the free MetAP-2 ~~in the biological sample~~ reacts with the quantifiable irreversible Metap-2 inhibitor to form a MetAP-2/inhibitor complex; and
(ii) determining the amount of MetAP-2/inhibitor complex produced in step (i).

8. (Currently Amended) The method of claim 1 wherein each of the plurality of biological samples is selected from the group consisting of whole blood, a blood fraction, erythrocytes, white blood cells, T-cells, B-cells, macrophages; tumor tissue; cancer cells; bone marrow; synovium, synovial fluid, cerebrospinal fluid; liver tissue; brain tissue; prostate tissue, breast tissue, lymph node tissue and spleen.

9. (Currently Amended) The method of claim 1 further including the step of lysing the cells in each of the plurality of biological samples following step (b).

10. (Currently Amended) The method of claim 1 further comprising the step of homogenizing each of the biological samples, or a portions thereof ~~of the biological sample~~ following step (b).

11. (Original) The method of Claim 6 wherein the test compound inhibits MetAP-2 activity *in vitro*.

12. (Original) The method of Claim 11 wherein the test compound is an irreversible inhibitor of MetAP-2.

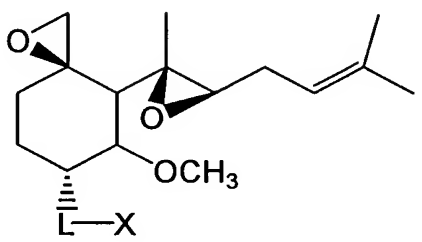
13. (Original) The method of Claim 12 wherein the test compound is a covalent inhibitor of MetAP-2.

14. (Original) The method of Claim 13 wherein the test compound is a fumagillin analogue.

15. (Currently Amended) The method of Claim 6 ~~Claim 1~~ wherein the ~~quantifiable irreversible~~ MetAP-2 inhibitor is a fumagillin analogue.

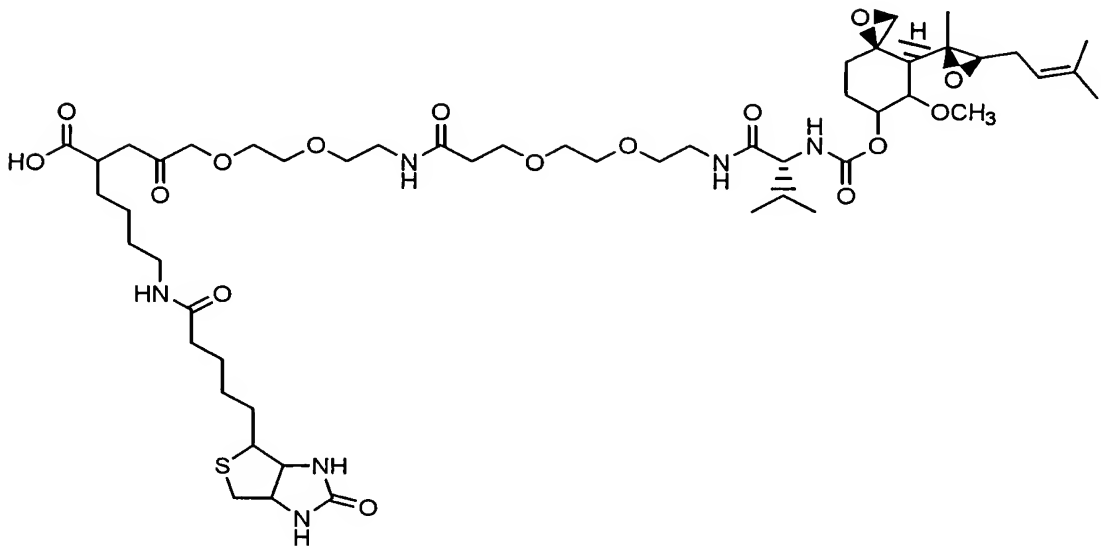
16. (Original) The method of Claim 15 wherein the fumagillin analogue comprises a biotin moiety.

17. (Currently Amended) The method of Claim 16 wherein the fumagillin analogue is of the structure:



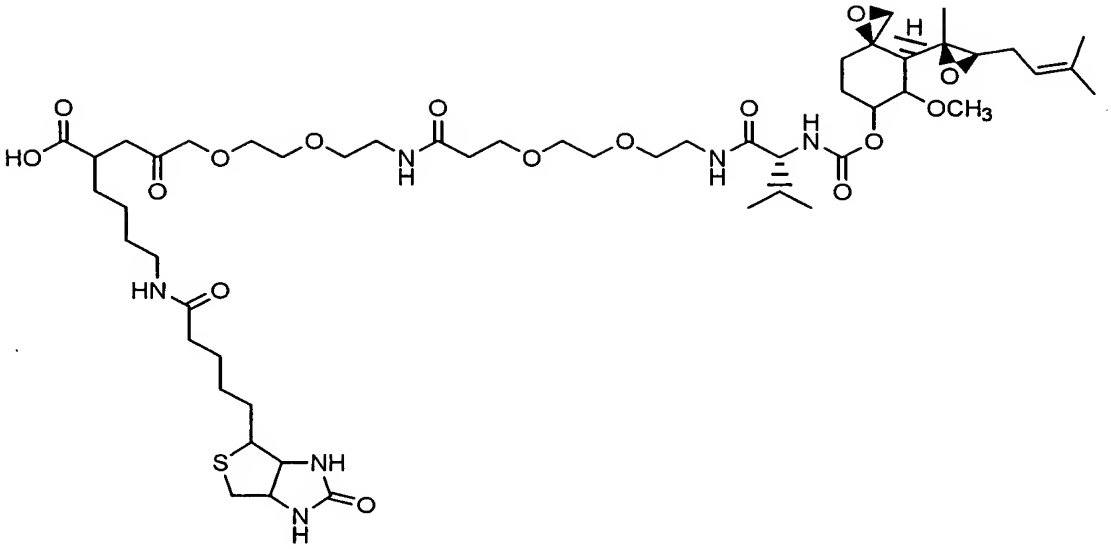
, wherein L is a linker group and X is a biotinyl moiety.

18. (Currently Amended) The method of Claim 17, wherein the fumagillin analogue is of the structure:



19.-25. (Canceled)

26. (New) A method for determining the extent of inactivation of MetAP-2 in a biological sample, or fraction thereof, derived from a subject, comprising the steps of:
(a) administering a test compound which is an inhibitor of MetAP-2 to the subject, wherein any MetAP-2 in the body of the subject that reacts with the test compound is inactivated MetAP-2 and any MetAP-2 that does not react with the test compound is free MetAP-2, wherein the MetAP-2 inhibitor is of the structure



;

(b) removing a plurality of biological samples from the subject, wherein each of the plurality of biological samples is derived from a different tissue of the subject; and

(c) determining the amount of free MetAP-2 within each of plurality of the biological samples, or a fractions thereof; and

(d) comparing the amounts determined in step (c) with the amount determined in a control sample;

wherein a decrease in the amounts in each of the biological samples determined in step (c) compared to the amount determined in step (d) is a measure of the extent of inactivation of MetAP-2 in each of the biological samples, or fractions thereof.